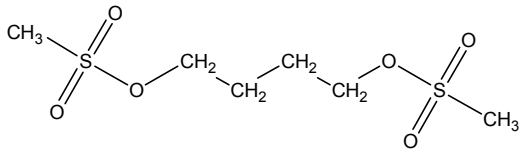
1,4-BUTANEDIOL DIMETHANESULFONATE (MYLERAN®)
CAS No. 55-98-1

First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

1,4-Butanediol dimethanesulfonate (Myleran®; busulfan) is *known to be a human carcinogen* based on is sufficient evidence of carcinogenicity in humans (IARC S.4, 1982; IARC S.7, 1987). Patients receiving 1,4-butanediol dimethanesulfonate treatment developed leukemia as well as cytological and hematological abnormalities.

An IARC Working Group reported that there is limited evidence of carcinogenicity of 1,4-butanediol dimethanesulfonate (Myleran®; busulfan) in experimental animals (IARC S.4, 1982; IARC S.7, 1987). When administered intraperitoneally, one study reported that 1,4-butanediol dimethanesulfonate induced T-cell lymphomas in male mice; two other studies reported that it did not increase the incidence of tumors. When administered by intravenous injection, 1,4-butanediol dimethanesulfonate increased the incidence of thymic lymphomas and ovarian tumors in female mice (IARC V.4, 1974; IARC S.4, 1982; IARC S.7, 1987). One study reported that pulmonary lesions developed in mice treated with 1,4-butanediol dimethanesulfonate but the route of administration was not specified. 1,4-Butanediol dimethanesulfonate administered intravenously induced a variety of tumors in male rats, but an IARC Working Group reported that the experiments could not be evaluated because of a lack of information.

PROPERTIES

1,4-Butanediol dimethanesulfonate is a white crystalline powder that is very slightly soluble in water and acetone. It is an active alkylating agent that hydrolyzes in water. When heated to decomposition, it emits toxic fumes of sulfur oxides (SO_x). The commercial product contains a minimum of 98% 1,4-butanediol dimethanesulfonate.

USE

1,4-Butanediol dimethanesulfonate is used as a chemotherapeutic agent taken orally to treat polycythemia and some forms of leukemia, particularly chronic myelocytic leukemia (IARC V.4, 1974; IARC S.4, 1982).

PRODUCTION

One U.S. company is known to produce an unknown quantity of 1,4-butanediol dimethanesulfonate and has produced it since 1954 (SRIa, 1986, 1997). Total annual production

was believed to be less than 1,102 lb in 1974 (IARC V.4, 1974). No data on imports or exports were available.

EXPOSURE

The primary routes of potential human exposure to 1,4-butanediol dimethanesulfonate are ingestion, inhalation, and dermal contact. Patients are exposed to 1,4-butanediol dimethanesulfonate during its use in chemotherapeutic treatment. Typical dosage level is 4 to 8 mg daily (IARC V.4, 1974). Potential occupational exposure may occur for workers formulating or packaging the tablets and for health care professionals administering the tablets. The National Occupational Exposure Survey (1981-1983) estimated that a total of 1,763 workers, including 893 females, potentially were exposed to 1,4-butanediol dimethanesulfonate (Myleran®) (NIOSH, 1984).

REGULATIONS

1,4-Butanediol dimethanesulfonate is a pharmaceutical used in relatively small amounts; therefore, it is of little regulatory concern to EPA. However, there may be a small pollution problem relative to hospital wastes. FDA regulates 1,4-butanediol dimethanesulfonate under the Food, Drug, and Cosmetic Act (FD&CA) as a prescription drug approved for human use. FDA requires warning labels on drugs containing 1,4-butanediol dimethanesulfonate concerning potential carcinogenicity, mutagenicity, teratogenicity, and/or impairment of fertility. OSHA regulates 1,4-butanediol dimethanesulfonate as a chemical hazard in laboratories under the Hazard Communication Standard. Regulations are summarized in Volume II, Table A-12.